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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/689,911	10/11/2000	C. Alexander Turner JR.	LEX-0068-USA	9082

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EXAMINER	
BUNNER, BRIDGET E	

ART UNIT	PAPER NUMBER
1647	10

DATE MAILED: 03/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/689,911	Applicant(s) TURNER ET AL.	
	Examiner Bridget E. Bunner	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-4* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5, 6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Sequence Compliance

The Applicant's response to the Notice to Comply with Sequence Listing Requirements under 37 CFR §1.821 (Paper No. 8, 29 January 2002) has been considered and is found persuasive. Therefore, the requirements set forth in the Notice to Comply (Paper No. 7, 03 December 2001) are withdrawn.

Oath/Declaration

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

Specification

2. The disclosure is objected to because of the following informalities:

2a. Patent applications are referenced in the disclosure (pg 12, line 23). The status of the applications must be updated.

2b. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "NUCLEIC ACID MOLECULE ENCODING A HUMAN GALANIN FAMILY PROTEIN".

Appropriate correction is required.

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation.

Specifically, claims 1-4 are directed to an isolated nucleic acid molecule comprising at least 24 contiguous bases of nucleotide sequence disclosed in the NHP polynucleotides described in SEQ ID NO: 1. The claims also recite an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a novel amino acid sequence of at least about 29 amino acids in length and that initiates at amino acid number 33 of SEQ ID NO: 2 or a nucleotide sequence that encodes the amino acid sequence shown in SEQ ID NO: 2.

The specification discloses that the "present invention relates to the discovery, identification, and characterization of novel human polynucleotides encoding proteins that share sequence similarity with mammalian galanins" (pg 1, lines 8-11). The specification also teaches that galanins are associated with "regulating body weight, modulating behavior, treating pain, inflammation, neuronal repair, Alzheimer's dementia, inflammatory bowel disorders, and infectious disease" (pg 1, lines 32-36). However, the instant specification does not teach any

significance or functional characteristics of the human polynucleotide (SEQ ID NO: 1) or polypeptide (SEQ ID NO: 2). The specification also does not disclose any methods or working examples that indicate the polynucleotide and polypeptide of the instant invention are involved in any of the abovementioned activities. Since significant further research would be required of the skilled artisan to determine how the claimed polypeptide is involved any activity, the asserted utilities are not substantial. The specification asserts the following as patentable utilities for the claimed putative polynucleotide (SEQ ID NO: 1):

1) to inhibit or enhance the expression of novel human proteins (NHPs) (pg 2, lines 20-24)

2) to generate mutant nucleotides or chimeric fusion proteins (pg 3, lines 16-26; pg 8, lines 20-34)

3) as hybridization probes (pg 7, lines 13-37; pg 8, lines 1-19)

4) to create a genomic library or expression library (pg 8, lines 35-37; pg 9, lines 1-29)

5) to construct a transgenic animal (pg 2, lines 26-28)

6) in gene therapy (pg 11, lines 25-34)

Each of these shall be addressed in turn.

1) to inhibit or enhance the expression of novel human proteins (NHPs). This asserted utility is credible but not substantial or specific. Such can be performed for any polynucleotide. Further, the specification does not disclose specific cDNA, DNA, or RNA target sequences that would be utilized to inhibit or enhance protein expression. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

2) to generate mutant nucleotides or chimeric fusion proteins. This asserted utility is credible but not substantial or specific. Such assays can be performed with any polynucleotide. Further, the specification discloses nothing specific or substantial for the mutant polynucleotide or chimeric polynucleotide that is produced by this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

3) as hybridization probes. This asserted utility is credible but not substantial or specific. Hybridization probes can be designed from any polynucleotide sequence. Further, the specification does not disclose specific cDNA, DNA, or RNA targets. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) to create a genomic library or an expression library. This asserted utility is credible but not specific or substantial. Such can be performed for any polynucleotide. Further, the specification does not disclose a specific nucleic acid sequence used to generate the library. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

5) to construct a transgenic animal. This asserted utility is credible but not specific or substantial. The specification does not disclose diseases associated with a mutated, deleted, or translocated gene of the instant application (SEQ ID NO: 1). Significant further experimentation would be required of the skilled artisan to identify such a disease. The specification discloses nothing about whether the gene will be "knocked in" or "knocked out" or what specific tissues

and cells are being targeted. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

6) in gene therapy. This asserted utility is not credible, specific or substantial. Such can be performed for any polynucleotide. Further, the specification does not disclose diseases associated with a mutated, deleted, or translocated gene of the instant application (SEQ ID NO: 1). Significant further experimentation would be required of the skilled artisan to identify individuals with such a disease. Since this asserted utility is also not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4. Claims 1 and 4 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, claims 1 and 4 are directed to an isolated nucleic acid molecule comprising at least 24 contiguous bases of nucleotide sequence disclosed in the NHP polynucleotides described in SEQ ID NO: 1. The claims also recite an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a novel amino acid sequence of at least about 29 amino acids in length and that initiates at amino acid number 33 of SEQ ID NO: 2.

The specification teaches that corresponding NHP homologues from other species are encompassed by the invention. The specification also discloses that "any NHP protein encoded by the NHP polynucleotide sequences described above are within the scope of the invention, as are any novel polynucleotide sequences encoding all or any novel portion of an amino acid

sequence presented in the Sequence Listing" (pg 13, lines 8-15). However, the specification does not teach any variants or fragments of the polynucleotide (SEQ ID NO: 1) of the instant application. The specification also does not teach functional or structural characteristics of the polynucleotide or polypeptide fragments recited in the claims.

The problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the polynucleotide and protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is

dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone (Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

5. Claims 1 and 4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 4 recite an isolated nucleic acid molecule comprising at least 24 contiguous bases of nucleotide sequence disclosed in the NHP polynucleotides described in SEQ ID NO: 1. The claims also recite an isolated nucleic acid molecule comprising a nucleotide sequence that

encodes a novel amino acid sequence of at least about 29 amino acids in length and that initiates at amino acid number 33 of SEQ ID NO: 2.

The specification teaches a novel human protein (NHP) polynucleotide (SEQ ID NO: 1) and a polypeptide encoded by the nucleotides of SEQ ID NO: 1. However, the specification does not teach functional or structural characteristics of the polynucleotides in the context of a cell or organism. The description of one polynucleotide species (SEQ ID NO: 1) and one polypeptide species (SEQ ID NO: 2) is not adequate written description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all variants and fragments and with at least 24 contiguous bases of SEQ ID NO: 1 or at least about 29 amino acids in length and that initiates at amino acid number 33 of SEQ ID NO: 2.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid

itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only an isolated nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 1 and an isolated nucleic acid molecule that encodes the amino acid sequence of SEQ ID NO: 2, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-2 and 4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 1 is rejected as being indefinite because the claim is missing words which render the meaning of the claim unclear. For example, in claim 1, lines 2-3, the phrase "at least 24 contiguous bases of nucleotide sequence first disclosed in the NHP polynucleotides described in SEQ ID NO: 1" is confusing. (Please note that this issue could be overcome by amending claim

1 to recite, for example: "at least 24 contiguous bases of the nucleotide sequence of SEQ ID NO: 1".

8. Claim 4 is rejected as being indefinite because the claim is missing words which render the meaning of the claim unclear. For example, in claim 4, lines 2-4, the phrase "encodes a novel amino acid sequence of at least about 29 amino acids in length that initiates at amino acid number 33 of SEQ ID NO: 2" is confusing. The specification and the claims do not disclose the significance of amino acid residue 33 of SEQ ID NO: 2.

8. Regarding claim 1, the acronym "NHP" renders the claims vague and indefinite. Abbreviations should be spelled out in all independent claims for clarity.

9. Claim 2 is rejected as being indefinite. Stringency is relative, and the art does not recognize a single set of conditions as stringent. The specification also does not provide an unambiguous definition for the term. In the absence of a recitation of clear hybridization conditions (e.g., "hybridizes at wash conditions of **A** X SSC and **B** % SDS at **C**°C"), claim 2 fails to define the metes and bounds of the varying structures of nucleotide sequences recited in the claimed methods.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

11. Claims 1 and 4 rejected under 35 U.S.C. 102(a) as being anticipated by Zhao et al. (Genbank Accession Number AQ549952).

Zhao et al. teach an isolated nucleic acid molecule comprising at least 24 contiguous bases of the nucleotide sequence of SEQ ID NO: 1 of the instant application (see sequence alignment attached to this Office Action as Appendix A; see nucleotides 378-502 of Adams et al.; see also nucleotides 220-344 of SEQ ID NO: 1 of the instant application). Zhao et al. also disclose an isolated nucleic acid molecule comprising a nucleotide sequence that encodes an amino acid sequence of at least 29 amino acids of SEQ ID NO: 2 (see sequence alignment attached to this Office Action as Appendix B; see nucleotides 375-500 of Zhao et al.; see also amino acids 73-114 of SEQ ID NO: 2 of the instant application).

Conclusion

No claims are allowable.

The art made of record and not relied upon is considered pertinent to applicant's disclosure:

Ohtaki et al. J Biol Chem 274(52): 37041-37045, 1999.

Ohtaki et al. WO 9948920

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

BEB
Art Unit 1647
March 5, 2002

ELIZABETH C. KEMMERER
PRIMARY EXAMINER